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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/378,045	08/20/1999	CHARLES RAUCH	2625-E	8651

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EXAMINER	
GAMETT, DANIEL C	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 02/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/378,045	RAUCH ET AL.	
	Examiner	Art Unit	
	Daniel C Gamett	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 Feb,. 2002, 10 Jun, 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38 and 40-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38 and 40-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on ____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *May 10, 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Listing Error Report* + Notice To Comply

DETAILED ACTION

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647. The Examiner for this Application is now Daniel C. Gamett.

2. This responds to the Amendment and Reply received 11 Feb. 2002 and to the Response to Notice to comply and Statement under 37 C.F.R. § 1.821(f) and (g) dated 10 June, 2002. The status query of December 22, 2004 is noted.

Specification

3. Amendment to the specification to recite "Brief Description of the Drawings" has been entered and the previous objection is withdrawn.

Sequence Rules

4. Amendments to Figures 1 and 5 and to the Brief Description of the Drawings to provide references to a sequence identifier have been entered. The instant application is still not fully in compliance with the sequence rules, 37 C.F.R. §§ 1.821-1.825. The sequence error report is attached for Applicant's convenience. The Examiner notes that the error found in the computer readable format also appears in the printed sequence listing. The errors in the printed sequence listing and computer readable format must be corrected.

5. The Examiner has used the sequences in the parent application number 08/883,036 to do a sequence search for SEQ ID NO:4, necessitated by the addition of new claims 40-73.

Status of the Claims

6. Claims 1-37 and 39 have been cancelled; claim 38 is amended, and new claims 40-73 have been entered in the amendment of 11 Feb 2002. Claims 38 and 40-73 are under consideration.

7. The amendment to claim 38 obviates the prior objection regarding improper dependency and so said objection is withdrawn.

8. In view of the amendment to claim 38, which now recites amino acids 52-440 of SEQ ID NO:2, rejection of claim 38 under 35 U.S.C. § 102(e) as being anticipated by Arizumi et al., (US Pat. No. 6,046,158), as set forth in the previous Office Action, is withdrawn.

Priority

9. The instant application is at the end of a series of continuations-in-part and therefore individual claims under consideration receive benefit of priority to different effective filing dates as follows.

10. The earliest effective filing date for claims 38, 41, 43-46, 48, 51-53, 55,57-60, 62, 64-67, 69, 71-73 is 03/28/1997. These claims are drawn to antibodies directed against a TRAIL-R with the following characteristics: (a) consisting of amino acids 51-440 of SEQ ID NO:2, (claims 38, 41 and their dependent claims); (b) comprising the amino acid sequence VPANEDG (claim 43 and its dependent claims); (c) comprising VPANEDG and having a molecular weight of about 50-55 kDa (claim 44 and its dependent claims); or (d) VPANEDG and the amino acids of SEQ ID NO:4 (claim 45 and its dependent claims). The earliest enabling written description of the polypeptide of SEQ ID NO:2 is in Application No. 08/829,536, filed 03/28/1997. The 02/13/1997 disclosure (ASN: 08/799,861) fails to provide adequate

written description because a skilled artisan would not know how to make the claimed antibody based on the information provided. The artisan would attempt to raise antibodies using the peptide sequences VPANEGD, VCEV, or SGEVELSSV. Of these, VCEV and SGEVELSSV are not found in SEQ ID NO:2, so not only do these sequences not provide any description that could be used to make an antibody directed against the polypeptide encoded by SEQ ID NO:2 , their use would actually hinder the process. Even though the proteins of which these peptides are part bind TRAIL, the particular TRAIL- binding protein recognized by a particular antibody could not be determined without considerable further research because of the paucity of information about the individual proteins in the specification. VPANEGD is indeed amino acids 327-33 of SEQ ID NO:2, but reliance on this peptide alone to raise an antibody specific for the polypeptide encoded by SEQ ID NO:2 would require undue experimentation, especially considering that TRAIL receptor DR4 contains a similar sequence, VPANGAD (positions 330-336 in Fig. 1A, Pan *et al.* Science 276:111 Apr 4, 1997, IDS item C9)). The disclosure dated 03/12/1997 (ASN 08/815,255) includes SEQ ID NO:4, now recited in claim 45, but it is not clear from that disclosure that VPANEGD and the peptide specified by SEQ ID NO:4 are actually part of the same polypeptide chain, so this disclosure does not provide support for instant claims 43-45. Furthermore, ASN 08/815,255 also recites VCEV and SGEVELSSV as being identifying peptides of the claimed polypeptide (p.19). Thus it appears that, as of 03/12/1997, Applicants were in possession of a mixture of partially characterized polypeptides that may have included the polypeptide encoded by SEQ ID NO:2 and that the disclosure dated 03/12/1997 neither provides a written description for the polypeptide encoded by SEQ ID NO:2 nor

enables one of skill in the art to make and identify the antibodies claimed in the instant application. Application No. 08/829,536, filed 03/28/1997 discloses the entirety of SEQ ID NO:2 as well as the nucleic acid sequence encoding it, and therefore provides written description and enablement for the genus of antibodies in claims 38, 41, 43-45 and claims dependent therefrom.

11. The earliest effective filing date for claims 40, 42, 47,49, 54,56,61,63, 68, and 70 is 06/05/1997. Claims 40 and 42 are drawn to antibodies that are directed to a polypeptide that consists essentially of amino acids x to 210 of SEQ ID NO:2 wherein x represents an integer from 51 to 59. The basis for the limitation to amino acids 52-210 was established in ASN 08/869,852, filed 06/05/1997 (p. 6, lines 1-6), which identified these amino acids as comprising the extracellular domain, suitable for expressing a soluble form of TRAIL-R. Disclosures made prior to 06/05/1997 provide neither a description nor a specific or substantial utility for the limitation that defines the species of antibodies in claims 40, 42, and claims dependent therefrom.

12. In summary, claims 38, 41, 43-46, 48, 51-53, 55,57-60, 62, 64-67, 69, and 71-73 receive benefit of priority to 03/28/1997 and claims 40, 42, 47,49, 54,56,61,63, 68, and 70 receive benefit of priority to 06/05/1997.

Claim Rejections 35 U.S.C. 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> a. A person shall be entitled to a patent unless –
>
> b. (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant

> for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 38, 40-52, and 60-73 are rejected under 35 U.S.C. 102(e) as being anticipated by Ni *et al.*, Publication No. 20020098550, July 25, 2002, Application No. 09/ 005842 (IDS item A20). Ni et al., disclose DR5, a 411 amino acid transmembrane protein that binds TRAIL. The TRAIL-R of the instant specification and DR5 are alternative splice variants of the same gene product; amino acids 183-213 of TRAIL-R are not found in DR5, otherwise their amino acid sequences (SEQ ID NO:2 in each case) are identical. Ni *et al.*, teach the production of antibodies to DR5 or fragments thereof at section [0139]. Thus, Ni *et al.* anticipate antibodies to a polypeptide that binds TRAIL comprising VPANEGD (as in claim 43), having a molecular weight if about 50-55 kD (as in claim 44), further comprising the amino acid sequence of SEQ ID NO:4 (as in claim 45), and to fragments of the polypeptide of SEQ ID NO:2 that are capable of binding TRAIL (as in claims 38 and 41). The antibodies taught by Ni et al. would inherently recognize the soluble extracellular domain polypeptides of claims 40 and 42. The polypeptide and nucleic acid sequences of DR5 as well as antibodies to DR5 are fully disclosed in priority document, Provisional Patent application 60/040846, filed 3/17/1997 (IDS item A3). The antibodies taught include monoclonal antibodies (sections[0121] and [138]), as well as antibodies conjugated to a detectable or therapeutic moiety (section [0130]).

Claim Rejections 35 U.S.C. 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 53-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ni *et al.*, Publication No. 20020098550, July 25, 2002, Application No. 09/ 005842, as applied to claims 38, 40-52, and 60-73 above, and further in view of Hoogenboom, et al.. PAT 5,565,332, October 15, 1996. Claims 53-59 are drawn to humanized antibodies directed against the TRAIL-R polypeptide. As described above, Ni *et al.*, teach polyclonal, monoclonal, and conjugated antibodies to the identical polypeptide. Ni *et al.*, do not teach humanized antibodies as recited in the instant claims. Hoogenboon et al, teach in column 1, lines, 24-56, that humanization of monoclonal antibodies was already a highly developed art at their filing date and the remainder of their disclosure teaches an improved procedure therefore. It would have been obvious to one of skill in the art at the time the instant invention was made to combine the teachings of Ni et al, which provide antibodies to the DR5/TRAIL-R polypeptide with the teachings of Hoogenboom et al, to provide humanized antibodies, with a reasonable expectation of success. Motivation to do so would comes from the well-known advantages of humanized antibodies for therapeutic use in humans, principally the absence of non-human polypeptide structures that can provoke an immune response.

Conclusion

17. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D., whose telephone number is 571 272 1853. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DCG
Art Unit 1647
4 February 2005

CHRISTINE J. SAOUD
PRIMARY EXAMINER